Remarks/Arguments

Claims 1-15 and 17 are pending in the application. Claims 1-9 and 15 have been withdrawn from consideration pursuant to a lack of unity objection. Claims 10-14 and 17 are therefore under consideration. Reconsideration is requested in view of the above changes and the following remarks.

The claims have been amended to point out that for the complexes of the invention formed between heat shock proteins and an antigenic peptide fragment derived from pathogenic bacteria, both the heat shock protein and the peptide fragment are derived from same cell, i.e., the pathogenic bacteria. This feature is supported by the specification at page 6, lines 11-24.

Response to Rejections Under 35 U.S.C. § 102

Srivastava (US Patent No 5,961,979) - Rejection Under 35 U.S.C. § 102(e)

The Examiner maintains the rejection of claims 10-14 and 17 as allegedly anticipated by Srivastava (US Patent No 5,961,979). Applicant respectfully submits that the claims, as presently amended, are not anticipated by Srivastava for the following reasons.

It is well settled that "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." MPEP §2131 (quoting Verdegaal Bros. v. Union Oil Co. of Calif., 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)). "The identical invention must be shown in as complete detail as is contained in the . . . claim." Id. (quoting Richardson v. Suzuki Motor Co., 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). Therefore, when taken alone, Srivastava must describe each and every element of each of amended claims 10 and 11, and dependent claims 12-14 and 17 in order to anticipate the claims under 35 U.S.C. § 102(e). However, Srivastava does not meet this burden.

Srivastava teaches "the use of *mammalian* HSP-complexes from infected cells as vaccines against intracellular pathogens." It is this distinction which differentiates the presently-claimed invention from Srivastava. Specifically, the instant claimed invention encompasses complexes comprising a heat shock protein complexed to a peptide fragment. Both the heat shock protein and the antigenic fragment are derived from the same cell, a pathogenic bacterium.

Srivastava discloses complexes which are fundamentally different and therefore distinct from the complexes of the present invention. In particular, the heat shock protein + peptide complexes which are taught by Srivastava include a heat shock protein component which is derived from a host cell which has been infected by a bacterial pathogen, this "host cell" derived heat shock protein being complexed with a peptide which is derived from the pathogenic cell, which is infecting the host cell.

Accordingly, Srivastava does not teach a heat shock protein/peptide complex which is produced in-situ within the pathogenic bacteria. Rather, the complexes of Srivastava are formed within the "host" cell which is being infected by the bacterial pathogen. The heat shock protein/peptide complexes which are taught by Srivastava are therefore not "endogenous" to the pathogenic bacteria, as claimed in the instant invention.

The examples provided in Srivastava illustrate examples in which an antigenic peptide is produced recombinantly within a host cell. However, the host cell of Srivastava is a mammalian cell, and accordingly, the complexes which result comprise mammalian cell-derived heat shock proteins which are complexed to antigenic peptide fragments which are produced recombinantly within the "host" cell. Accordingly, the complexes which result are not endogenous complexes derived from a bacterial pathogen. As such, the teachings of Srivastava are limited to the isolation of heat shock protein/peptide complexes derived from pathogen-infected host cells, and the use of these heterogeneous-source complexes as vaccines.

The fact that Srivastava does not teach the complexes of the presently-claimed invention is also evidenced in text related to "Preparation of Stress Proteins and Immunogenic Stress Protein-Peptide Complexes" as taught in Srivastava at column 13, lines 51 to 67. In particular, the use of a dounce homogenizer as taught at line 63 would only disrupt infected mammalian cells, and not bacterial pathogens, as bacterial pathogens would be too small in size to be disrupted using this technique. One of ordinary skill in the art would recognize this and also know that the bacterial pathogens would be present in the "other debris" component as taught at line 65 of column 13, which results from the subsequent centrifugation which removes unbroken cells (lines 64 to 66).

Furthermore, the use of ATP-agarose chromatography, as taught in column 14, line 35, would result in the isolation of heat shock proteins and not heat shock protein-peptide complexes, as the ATP causes the complex to dissociate, particularly where ATP is used to elute (as taught at line 46 of column 14).

The reference made by the Examiner to column 3, lines 36-37 and 43-45 of Srivastava, relating to a generic description of a subunit vaccine is, in fact, located in the Background of the Invention section of the patent, and do not describe components of the invention as described in detail in Srivastava. Furthermore, the references made by the Examiner to column 5, line 57 of Srivastava, in relation to heat shock proteins other than mammalian heat shock proteins, are in no way relevant to the overall teaching of Srivastava. Rather, these passages also merely provide general information relating to the background of the invention.

There is therefore no teaching in Srivastava that a heat shock protein derived from a non-mammalian cell can be used in the invention of Srivastava. There is also no teaching in Srivastava that the heat shock protein + peptide complex can be derived from a heat shock protein and a peptide which are both derived from the same cell, where the cell is a bacterial pathogen.

To the contrary, Srivastava only discloses the peptide portion of the complex as being expressed in a mammalian cell. This argument is supported by column 9, line 24 of Srivastava, which sets forth that the Srivastava invention relates to the isolation of complexes derived from a eukaryotic cell, and is further supported by the claims of Srivastava, which are directed only to complexes derived from mammalian cells.

Applicant respectfully contends that the mere recitation of a prokaryotic heat shock protein in the background section of Srivastava does not constitute a teaching by Srivastava of the specifically-claimed heat shock protein complexes of the present invention. There is no basis in Srivastava for such a conclusion to be drawn, for at no time does Srivastava suggest that the heat shock protein component of the complexes taught in Srivastava can be derived from a cell type other than an eukaryotic cell.

Accordingly, the endogenous bacterial pathogen derived complexes claimed in the present invention are not disclosed or taught by Srivastava. Accordingly, Applicant submits that claims 10-14 and 17 are not anticipated by Srivastava, and requests that the rejection be reconsidered and withdrawn.

Phipps et al. (1991, EMBO J., 10:1711-1722) - Rejection Under 35 U.S.C. § 102(b)

The Examiner rejected claims 10-14 and 17 as allegedly being anticipated by Phipps et al. Applicants respectfully submit that Phipps et al. does not teach the amended claims for the following reasons.

Applicant submits that Phipps et al. contains no teaching that an in-situ complex can be formed between a heat shock protein which has been induced in a bacterial cell, following the exposure of that cell to heat shock and a peptide which is also present in that cell, such that the resulting complex can be used to illicit an immune response.

The complex in Phipps et al. which is identified by the Examiner as being induced by heat shock is almost completely uncharacterized, other than the fact that the expression of the complex of Phipps et al. results following heat shock. The authors state in the last paragraph on page 1719 of Phipps et al. that "We do not know what the function of the ATPase function is". It is therefore not known whether the molecule will complex with peptide fragments. Any similarity with heat shock proteins is purely speculative based on loose structural homology, and furthermore, it is not known whether the protein will even complex with a peptide and whether the resulting composition will illicit an immune response. The skilled artisan would understand that such findings as disclosed by Phipps et al. is, at best, an invitation for further experimentation.

Accordingly, as there is no teaching of an immunogenic or binding function of the protein identified in Phipps et al., and further, because there is no teaching of such protein complexed with a peptide fragment, as is claimed in the instant invention, there is therefore no disclosure of a composition which is set forth in the claims of the instant application. Accordingly, Phipp et al. does not teach "each and every element" of the presently-claimed invention, as required under 35 U.S.C. § 102(b). Applicant submits that claims 10-14 and 17 are not anticipated by Phipps et al., and requests that the rejection be reconsidered and withdrawn.

Wawrzynow et al. (1991, EMBO J., 9:1867-1877) - Rejection Under 35 U.S.C. § 102(b)

The Examiner rejected claims 10 and 11 as allegedly being anticipated by Wawrzynow et al. Applicants respectfully submit that Wawrzynow et al. does not teach the amended claims for the following reasons.

There is no teaching or consideration in Wawrzynow et al. that the ClpX heat shock protein can be administered to a subject in order to illicit and immune response against said heat shock protein. Rather, ClpX is considered purely as a molecular chaperone protein. Because there is no teaching provided in Wawrzynow et al. of a composition as defined in amended claim 10 or

11, Wawrzynow et al. does not teach each and every element of claims 10 and 11, as required under 35 U.S.C. § 102(b). Accordingly, Applicant submits that amended claims 10 and 11 are not anticipated by Wawrzynow et al., and requests reconsideration and withdrawal of the rejection.

Rambukkana et al. (1992, Infec. Immun., 60:4517-4527) - Rejection Under 35 U.S.C. 102(b)

The Examiner has rejected claim 10 under 35 U.S.C. § 102(b) as being anticipated by Rambukkana et al. Applicant respectfully submits that Rambukkana does not anticipate amended claim 10 for the following reasons.

The teachings of Rambukkana et al. are focused on the presence of cross-reactive epitopes which are present on heat shock proteins. One of ordinary skill in the art, having considered the teachings of Rambukkana, would find that only a heat shock protein was necessary to induce an immune response. The cross-reactive epitopes taught by Rambukkana et al. demonstrate that the complexing of a peptide to the heat shock protein would not be of relevance in mediating an immune response.

The endogenous complexes set forth in claim 10 are not disclosed in Rambukkana et al., as there is no teaching in Rambukkana et al. of the use of a complex of a heat shock protein-peptide complex in mediating an immune response. Rather, any immune response which results would, based on the teachings of Rambukkanna et al., be derived from one of the three unique epitopes present on the heat shock proteins which are analyzed therein. Furthermore, there is no consideration of inducing the expression of these proteins by heat shock in order to modulate the peptides which the resulting induced heat shock proteins would complex with.

Accordingly, Applicant submits that amended claim 10 is not anticipated by Rambukkana et al., and requests reconsideration and withdrawal of the rejection.

Motohashi et al. (1999, PNAS, 96:7184-7189) - Rejection Under 35 U.S.C. 102(a)

The Examiner has rejected claim 10 under 35 U.S.C. § 102(a) as being anticipated by Motohashi et al. Applicant respectfully submits that Motohashi et al. does not anticipate amended claim 10 for the following reasons.

Motohashi relates generally to the disclosure of the function of chaperone proteins. It does not teach the function of these chaperones as being "heat-induced" and in turn complexing with antigenic peptides, which complexes can then be used to illicit immune responses.

Furthermore, the focus of the chaperones discussed relates to Hsp70 and Hsp104 derived from eukaryotic cells. The present invention, as claimed, relates to the expression of heat shock proteins produced by bacterial pathogens following their exposure to heat shock in order to obtain complexes which result from these induced heat shock proteins complexing with proteins which are present within the bacterial pathogen cell (i.e., "endogenous" complexes).

Accordingly, the skilled artisan, armed with the teachings of Motohashi et al., would not arrive at the composition as defined in amended claim 10 of the instant invention. Accordingly, Applicant submits that amended claim 10 is not anticipated by Motohashi et al., and requests reconsideration and withdrawal of the rejection.

Obviousness-Type Double Patenting Rejection

The Examiner has provisionally rejected claims 10, 12 and 17 on the grounds of nonstatutory obviousness-type double patenting. The Examiner is of the opinion that claims 10, 12 and 17 are unpatentable over claims 1, 3 and 12 of copending Application No. 10/363,454. Applicant requests that the provisional nonstatutory double patenting rejection be placed in abeyance until claims have actually issued or are deemed allowable in one of the applications.

Conclusion

The claims remaining in the application are believed in condition for allowance. An early action toward that end is earnest solicited.

Respectfully submitted

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